Attached hereto is a marked-up version of the changes made by the current amendment. The attached pages are captioned **"Version with Markings to Show Changes Made"**.

INFORMATION DISCLOSURE STATEMENT

In the Office Action, the Examiner noted that no Information Disclosure Statement has been filed with the instant application. In response, Applicants are in the process of preparing the Information Disclosure Statement in accordance with 37 C.F.R. §1.56, 1.97 and M.P.E.P. § 2000 and will submit the IDS shortly.

COMPLIANCE WITH THE SEQUENCE RULES

In the Office Action, the Examiner noted that the Amendment filed on August 16, 2001 with the sequence listing did not contain a statement that the content of the paper and CRF copies include no new matter as required by 37 C.F.R. 1.821 through 1.825. In response, Applicants hereby submit a statement as required by 37 C.F.R. 1.821 through 1.825.

OBJECTIONS TO THE SPECIFICATION

In the Office Action, the Examiner objected to the specification as allegedly improperly incorporating required materials by reference. In response, as requested by the Examiner, the specification has been amended to include a description of the isolation of the rat pHyde gene as described in U.S.Serial No. 09/302,457, page 82, lines 9-14 which was incorporated by reference. Therefore, Applicants respectively request that the Examiner withdraw the objection.

Further, in the Office Action, the Examiner objected to the Abstract because the Abstract cannot be titled "Abstract of the Invention". In response, the Applicants have amended the Abstract. Therefore, Applicants respectively request that the Examiner withdraw the objection.

Lastly, in the Office Action, the Examiner objected to the title for not describing the claimed subject matter. In response, the title has been amended. Therefore, Applicants respectively request that the Examiner withdraw the objection.

REJECTIONS ON THE 35 U.S.C. § 112 SECOND PARAGRAPH

In the Office Action, the Examiner asserted that claims 1, 7, 10-27, 54-57, and 59-60 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the phrase "an isolated nucleic acid".

In response, claims 1, 7, 10-11, 16-19, 54-57 and 59-60 have been amended to overcome the antecedent basis deficiencies noted by the Examiner. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Applicants respectfully request that the Examiner reconsider and withdraw the rejections.

Further, in the Office Action, the Examiner rejected claims 1, 7, 10-27, 54-57, and 59-60 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the term" analogs".

In response, Applicants submit that the term "analogs" is well known to the skill person in the art. Further, the instant specification teaches and provides for analogs of the claimed isolated nucleic acid molecule which encodes a p-Hyde protein. Applicants traverse the Examiner rejection and respectfully request the Examiner to reconsider and withdraw the rejections.

Further, in the Office Action, the Examiner rejected claim 19 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the phrase "operatively, or an expression element linked to the nucleic acid".

In response, claim 19 has been amended. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Applicants respectfully request that the Examiner reconsider and withdraw the rejections.

Further, in the Office Action, the Examiner rejected claims 21-24 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the abbreviations "BAC" and "P1".

In response, claim 21 has been amended. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Applicants respectfully that the Examiner reconsider and withdraw the rejections.

Further, in the Office Action, the Examiner rejected claims 23-24 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by unclearly describing the adenovirus vector.

In response, claim 23 has been amended. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Applicants respectfully request that the Examiner reconsider and withdraw the rejections.

Lastly, in the Office Action, the Examiner rejected claims 54-56 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to

the term "similarity". In response, claims 54-56 have been amended. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Applicants respectfully request that the Examiner reconsider and withdraw the rejections.

REJECTIONS ON 35 U.S.C. § 112 FIRST PARAGRAPH

In the Office Action, the Examiner rejected claims 1, 7, 10-27, 54-56 and 59 under 35 U.S.C. § 112, first paragraph as allegedly failing to clearly define a structural limitation of the claimed nucleic acid sequences. In response, Applicants traverse the Examiner rejection. Applicants maintain that the claims are definite and particularly point out and distinctly claim Applicant's invention. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejections.

REJECTIONS ON THE 35 U.S.C. § 101

In the Office Action, the Examiner rejected claims 1, 7, 10-27, 54-57 and 59-60 under 35 U.S.C. § 101 as allegedly lacking patentable utility.

In response, Applicants respectfully traverse the Examiner's rejection. Applicants contents that the subject matter defined by the claims, namely the isolated nucleic acid molecule set forth in SEQ ID No. 1 is functionally and structurally characterized in the subject Application. Applicants have shown through experiments presented in the subject Application that the isolated nucleic acid molecule of the subject application has the ability to induce cell-death-susceptibility in a cancer cell. Therefore, the claimed isolated nucleic acid molecule has a credible patentable utility. Accordingly, Applicants respectfully request that the rejection of claims 1, 7, 10-27, 54-57 and 59-60 under 35 U.S.C. § 101 be reconsidered and withdrawn.

REJECTIONS ON 35 U.S.C. § 102

In the Office Action, the Examiner rejected claims 1, 7, 12, 13, 16 and 17 under 35 U.S.C. § 102(b), as allegedly being anticipated by Hillier et al.

In response, Applicants respectfully traverse this rejection. The Examiner asserted that Hillier et al. disclose "a human mRNA EST sequence that matches 155 nucleotides of Applicans' SEQ ID No:1". The Examiner admits that Hillier et al. does not disclose the isolated nucleic acid molecule as set forth in SEQ ID No. 1. Therefore, Hillier et al., as admitted by the Examiner cannot anticipate claim 1, as amended. Accordingly, Applicants respectfully assert that amended independent claim 1 is allowable.

Claims 7, 12, 13, 16 and 17 depend from, directly or indirectly, claim 1, and therefore include all the limitations of this claim. Therefore, Applicants resepectfully assert that claims 7, 12, 13, 16 and 17 are likewise allowable. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections to amended independent claim 1 and to claims 7, 12, 13, 16 and 17 dependent thereon.

Further, in the Office Action, the Examiner rejected claims 1, 7, 10-21, 25-27, 54-56 and 59 under 35 U.S.C. § 102(b), as being anticipated by Talerman et al.

In response, Applicants respectfully traverse this rejection. The Examiner asserted that Talerman et al. disclose " a DNA sequence that is 72% similar and 39% identical to Applicants' SEQ ID No:1". The Examiner admitted that Talerman et al. does not disclose the isolated nucleic acid molecule as set forth in SEQ ID No. 1. Therefore, Talerman et al., as admitted by the Examiner cannot anticipate claim 1, as amended. Accordingly, Applicants respectfully assert that amended independent claim 1 is allowable.

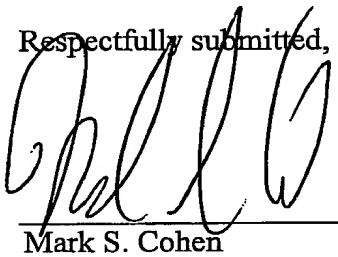
Claims 7, 10-21, 25-27, 54-56 and 59 depend from, directly or indirectly, claim 1, and therefore include all the limitations of this claim. Therefore, Applicants resepectfully assert that claims 7, 10-21, 25-27, 54-56 and 59 are likewise allowable. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections to amended independent claim 1 and to claims 7, 10-21, 25-27, 54-56 and 59 dependent thereon.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 05-0649.

Respectfully submitted,



Mark S. Cohen
Attorney for Applicant(s)
Registration No. 42,425

Dated: September 26, 2002

Eitan, Pearl, Latzer & Cohen-Zedek
One Crystal Park, Suite 210, 2011 Crystal Drive
Arlington, VA, USA 22202-3709
Telephone: (703) 486-0600
Fax: (703) 486-0800

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Title, the following changes were made:

ISOLATED NUCLEIC ACID ENCODING P-HYDE PROTEIN [AND METHODS OF INDUCING SUSCEPTIBILITY TO INDUCTION OF CELL DEATH IN CANCER]

In the Abstract, the following changes were made:

ABSTRACT [OF THE INVENTION]

--This invention provides and isolated nucleic acid molecule of the human p-Hyde gene, which act as inhibitors of a DNA repair enzyme and induce susceptibility of cancer cells to cell death, [analogs, fragments, mutants, and variants thereof]. The invention provides polypeptides, fusion proteins, chimerics[, fusion proteins], antisense molecules, antibodies, and uses thereof. [Also, this invention is directed to a method of inducing susceptibility to apoptosis with p-Hyde, a method of suppressing tumor growth with p-Hyde, and a method of treating a subject with cancer with p-Hyde alone or in combination with radiation, chemotherapy, or UV mimetic drugs. The invention also relates to the therapy of human cancers, which have a mutation in the p-Hyde gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the p-Hyde gene for mutations, which are useful for diagnosing the predisposition to cancer]. --

In the Specification, the following changes were made:

Paragraph beginning at page 90, line 14, has been amended as follows:

Construction of AdRSVpHyde: A rat pHyde cDNA gene was isolated as [described in U.S. Serial No:09/302,457] follows: Radiolabeled MAT-LyLu cDNA population in the presence of vast excess amount of competitor non-radiolabeled AT-1 cDNA population was

used to identify cDNAs clones in the MAT-LyLu cDNA library (Rinaldy and Steiner, 1997). One of these cDNAs was novel and designated as *p-Hyde*. The prostate cancer associated *p-Hyde* cDNA was further characterized. After digestion with EcoRI, a 2.6 kb fragment which contains the 1467 bp full-length coding sequence of pHyde cDNA was subcloned under the control of a truncated RSV promoter (395 bp) into an E1/E3 deleted adenoviral shuttle vector. The resultant adenoviral shuttle vector was cotransfected into 293 cells with pJM17, an adenoviral type 5 genome plasmid, by calcium phosphate method. Individual plaques were screened for recombinant AdRSVpHyde by PCR using specific primers for both the RSV promoter and pHyde cDNA sequences. Single viral clones were propagated in 293 cells. The culture medium of the 293 cells showing the completed cytopathic effect (CPE) was collected, and the adenovirus was purified and concentrated by twice CsC12 gradient untracentrifugation. The viral titration and transduction were performed as previously described. The schematic diagram of AdRSVpHyde was illustrated in Fig. 1. The sequence of AdRSVpHyde is set forth in Figure 10 (SEQ ID NO: 5 and SEQ ID NO: 6).--

Paragraph beginning at page 77, line 32, has been amended as follows:

--**Characterization of cDNA**: *Sequencing-p-Hyde* cDNA was originally obtained as a [?]λZAP Uni XR clone, and was further subcloned into pBluescript SK vector through *in vivo* excision protocol as described (Stratagen, La Jolla, California). This double-stranded cDNA was further subjected for Dye Terminator Cycle Sequencing (Perkin Elmer, Foster City, California) using ABI 377 automatic DNA sequencer Version 3.0. The open reading frame of *p-Hyde* cDNA was determined using the DNA Strider program (Pasteur Institute, Paris). --

In the Claims, the following changes were made:

1. (Amended) An isolated nucleic acid molecule which encodes a mammalian p-Hyde protein, including variants, analogs and mutants thereof, said nucleic acid molecule set forth in SEQ ID No. 1 [which includes susceptibility of a cancer cell to cell death], [including fragments,].

7. (Amended) The isolated nucleic acid molecule of claim 1, wherein the nucleic acid is DNA, c-DNA or RNA.

10. (Amended) The isolated nucleic acid molecule of claim 1, wherein the nucleic acid is labeled with a detectable marker.

11. (Amended) The isolated nucleic acid molecule of claim 10, wherein the detectable marker is a radioactive, colorimetric, luminescent, fluorescent [marker,] or gold label.

12. (Amended) An oligonucleotide of at least 15 nucleotides capable of specifically hybridizing with [a] the molecule [sequence of the nucleic acid which encodes the human p-Hyde] of claim 1.

17. (Amended) An antisense molecule capable of specifically hybridizing with the isolated nucleic acid molecule of claim 1.

18. (Amended) A vector comprising the isolated nucleic acid molecule of claim 1.

19. (Amended) The vector of claim 18, further comprising [a promoter of RNA transcription operatively, or] a[n] [expression] regulatory element linked to the nucleic acid molecule.

20. (Amended) The vector of claim 18, wherein the [promoter] regulatory element comprises a bacterial, yeast, insect or mammalian promoter.

21. (Amended) The vector of claim 20, wherein the vector is a plasmid, cosmid, yeast artificial chromosome (YAC), BAC artificial chromosome, adenovirus, adeno-associated virus, retrovirus, P1[,] bacteriophage or eukaryotic viral DNA.

23. (Amended) The adenovirus vector of claim 22, wherein the adenovirus vector comprises an adenovirus genome wherein the p-Hyde gene is inserted within [having] a

deletion in the E1 and E3 region of the genome [and an inserion within the region of a nucleic acid encoding p-Hyde, allele, fragment or variant thereof under the control of a promoter].

[53.]54. (Amended) The isolated nucleic acid sequence of claim 1[, wherein the nucleic acid has a nucleic acid sequence] having at least 75% [similarity with] complementary to the nucleic acid [coding] sequence of SEQ ID NO[s]: 1 [or 3].

[54.]55. (Amended) The isolated nucleic acid sequence of claim 1[, wherein the nucleic acid has a nucleic acid sequence] having at least 85% [similarity with] complementary to the nucleic acid [coding] sequence of SEQ ID NO[s]: 1 [or 3].

[55.]56. (Amended) The isolated nucleic acid sequence of claim 1[, wherein the nucleic acid has a nucleic acid sequence] having at least 95% [similarity with] complementary to the nucleic acid [coding] sequence of SEQ ID NO[s]: 1 [or 3].

[56.]57. (Amended) The isolated nucleic acid sequence of claim 1[, wherein the nucleic acid fragment is] as set forth in SEQ ID NO[s]: 1 [or 3].

[58.]59. (Amended) The isolated nucleic acid sequence of claim 53, wherein the nucleic acid is cDNA or genomic DNA.

[59.]60. (Amended) The isolated nucleic acid sequence of claim 1[, wherein the nucleic acid encodes] encoding an amino acid sequence having the sequence as set forth in SEQ ID NO[s]: 2 [or 4].